Original Article

ANATOLIAN CURRENT MEDICAL

DOI: 10.38053/acmj.1347060

Anatolian Curr Med J. 2023;5(4):405-410

Evaluation of gynecology and gynecologic oncology cases who received massive blood transfusion: a tertiary center experience

İzzet Özgürlük, Hüseyin Levent Keskin

Department of Obstetrics and Gynecology, Ankara Etlik City Hospital, Ankara, Turkey

Cite this article as: Özgürlük İ, Keskin HL. Evaluation of gynecology and gynecologic oncology cases who received massive blood transfusion: a tertiary center experience. *Anatolian Curr Med J.* 2023;5(4):405-410.

Received: 21.08.2023 ◆ **Accepted**: 06.09.2023 ◆ **Published**: 27.10.2023

ABSTRACT

Aims: To examine the frequency, indications and results of massive blood transfusion in gynecology and gynecological oncology cases.

Methods: The data of 56 cases who were underwent massive blood transfusion and operated on for benign/ malignant pathology indications in the gynecology and gynecological oncology clinics between October 1, 2022 and August 1, 2023, within a period of 10 months, were retrospectively analyzed. Demographic data of the cases (age, gravida, parity, body mass index), indications for hospitalization, vital signs during hospitalization, hemoglobin (Hb), hematocrit (Htc), platelet and INR values, massive transfusion indications, transfused blood products (erythrocyte suspansion, fresh frozen plasma (FFP), pooled platelet suspension, cryoprecipitate, fibrinogen) and the length of stay in the intensive care unit and hospitalization were retrospectively screened and analyzed statistically. The statistical significance level was accepted as $p<0.05$.

Results: 56 (1.8%) of 3146 patients were received massive blood transfusion. Massive blood transfusion was given to 30 (1.4%) of 2093 inpatients in the gynecology clinic, while this rate was found to be 2.5% (26/1053) in gynecologic oncology patients. The time between the decision to start transfusion and total transfusion times were similar between the groups ($p>0.05$). However, when the decision for transfusion was made, the INR value was statistically significantly higher in gynecological oncology cases ($p=0.001$). While the amounts of erythrocyte suspension given were similar between the two patient groups (5.1±1.4 vs. 6.3±3.5 U, $p= 0.082$), FFP amounts were higher in the gynecologic oncology group (3.3±2.0 vs. 6.2±3.7 U, $p=0.001$). When the blood groups of the cases were examined, it was seen that the most common blood groups were O (+) (n= 18, 32.1%) and A (+) (n=16, 28.6%). The duration of stay in the intensive care unit and hospitalization of gynecological oncology cases was significantly longer in gynecological cases. While 1 of 56 patients who underwent massive blood transfusion died (gynecological oncology case), 55 patients were discharged.

Conclusion: Timely transfusion decision is safe and life-saving in massive hemorrhages.

Keywords: Gynecology, gynecologic oncology, massive blood transfusion

INTRODUCTION

Massive hemorrhage has been described in many different ways in the literature. A few of these are >10 units over 24 h; total blood volume replaced within 24 h; 50% of total blood volume replaced within 3 h; four units of red blood cells (RBCs) transfused within 4 h with active major bleeding of more than 150 ml/min; three units RBCs administered over 60 min.[1] The replacement of these amounts is considered as massive blood transfusion. In the Patient Blood Management Guide published by the Ministry of Health, in Turkey, massive transfusion for adults is considered if more than half of the blood volume is transfused within 4 hours or more than the total blood volume (approximately 70 ml/kg of blood volume in adults) within 24 hours.[2]

In this study, our aim is to examine the frequency and indications of massive blood transfusion in gynecology and gynecological oncology cases in a tertiary center, as well as to investigate whether there is a difference between this group in terms of demographic and clinical characteristics.

Corresponding Author: İzzet Özgürlük, iozgurluk@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License.

METHODS

The study was carried out with the permission of Ankara Etlik City Hospital No: 1 Clinical Researches Ethics Committee (Date: 16.08.2023, AEŞH-EK1-2023-482). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In our study, which was designed as a observational retrospective study, the data of 56 cases who were operated on for benign and malignant pathology indications and underwent massive blood transfusion in the gynecology and gynecological oncology clinics between October 1, 2022 and August 1, 2023 were retrospectively analyzed.

In this study, the criteria for massive blood transfusion were >10 U within 24 hours or 4 U of Erythrocyte suspension (ES) replacement within 4 hours massive hemorrhage. Demographic data of cases (age, gravida, parity, body mass index), indications for hospitalization, vital signs during hospitalization, hemoglobin (Hb), hematocrit (Htc), platelet and INR values, and massive transfusion indications from the hospital database and medical files, transfused blood products (erythrocyte suspension, fresh frozen plasma, pooled platelet suspension, cryoprecipitate, fibrinogen), and length of stay in the intensive care unit and hospital stay were recorded. After evaluating the data of all cases who underwent massive transfusion, the cases were divided into 2 groups as gynecological cases and gynecological oncology cases. Data were also compared between the 2 groups.

SPSS (Statistical Package for Social Sciences) for Windows version 22.0 software was used for the statistical analysis of the data obtained in our study Descriptive and categorical data were expressed as numbers (n) and percentage (%). The results of the continuous data were given as mean±SD, median, and minimum-maximum values. The mean values of the data according to the groups were made using the Independent Sample -T test. A p value of <0.05 was considered statistically significant.

RESULTS

In our study, in which the gynecology and gynecological oncology data of our hospital were examined retrospectively, it was observed that a total of 3146 patients were hospitalized in an 8-month period. 56 of these patients received massive blood transfusion and the rate was calculated as 1.78%. When we separate cases in terms of clinics, massive blood transfusion was adminestered to 30 (1.4%) of 2093 patients in the gynecology clinic, while this rate was found to be 2.5% (26/1053) in gynecologic oncology patients.

The mean age of the gynecological oncology cases was significantly higher than the gynecological cases (p=0.001). Gravida, parity, and body mass index (BMI) were similar between the two groups (p>0.05) (**Table 1**). The most common indication for hospitilazition was severe anemia (Hb<7 g/dl) (n=14, 46.7%) in gynecological cases due to severe abnormal uterine bleeding, which constitutes almost half of the cases. In gynecological oncology cases, the most common indication was ovarian cancer (n=14, 53.8%) (**Table 2**).

Hemoglobin (Hb) and hematocrit (Htc) levels at hospitalization were found to be significantly lower in gynecological cases (respectively 8.1±3.4 g/dl vs. 10.7±2.2 g/dl, p=0.002; 26.5%±9.5 vs 33.7±6.6%, p=0.002). In 30 (53.6%) of 56 cases who underwent massive blood transfusion, the Hb value was below 10 g/dl at the time of hospitalization. In 16 of them (28.6%), emergency transfusion was initiated due to the presence of severe anemia (Hb<7 g/dl) at the time of hospitalization without surgery-related bleeding. 14 of 16 cases were admitted to the gynecology clinic due to severe abnormal uterine bleeding. The remaining 2 cases were diagnosed with ovarian cancer and had severe anemia. The hospitalization Hb value of 16 patients with severe anemia was 5.3±1.4 (median: 5.7; min: 2.4- max: 7.0) gr/dl. Indications requiring massive blood transfusion in the remaining 40 cases are shown in **Figure**.

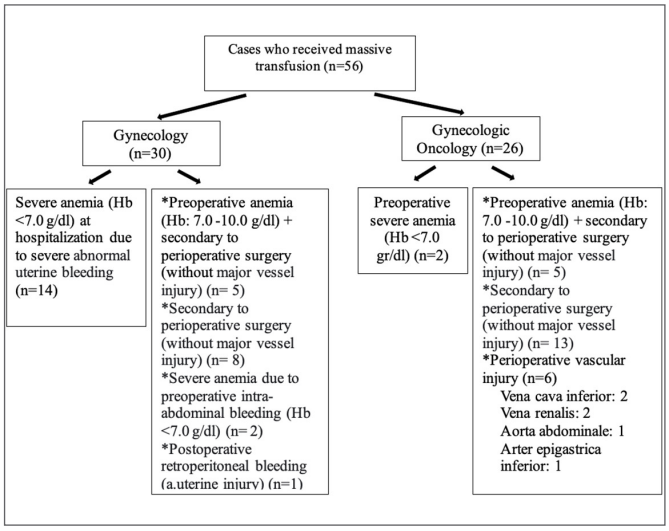

Figure. Indications for massive transfusion

Vital signs and shock index values were similar between clinics when deciding on transfusion due to surgery perioperatively (p>0.05). Likewise, the time between the decision to start transfusion and the total transfusion times were similar between the groups (p>0.05). However, the INR value was statistically significantly higher in gynecological oncology cases at the time of transfusion decision (p=0.001) (**Table 1**).

Table 1. Distribution of demographic, clinical and laboratory characteristics of cases

	All cases (n=56)	Gynecological cases (n= 30)	Gynecological oncology cases (n=26)	p
	Mean±SD (Median; minimum-maximum)	Mean±SD (min-max)		
Age	49.1±11.0 (49.0; 16 -73)	44.6±10.4 (25-69)	54.3±9.4 (38 -73)	0.001
Gravity (n)	3.0±2.5 (3; 0-13)	3.2±2.9 (0-13)	2.8±1.8 (0-8)	0.480
Parity (n)	2.7±1.4 (2; 0-7)	2.7±1.3 (0-6)	2.7±1.5 (0-7)	0.944
BMI (kg/m2)	28.3±5.9 (27.3; 18.7-43.0)	27.6±6.3 (18.7-43.0)	29.2±5.6 (20.0-42.5)	0.292
On admission to hospital				
Hb (g/dl)	9.3±3.2 (9.4; 2.4-14.7)	8.1±3.4 (2.4 -14.7)	10.7±2.2 (6.4-14.5)	0.002
HTC (g/dl)	29.9±9.0 (31.2; 10.5-47.0)	26.5±9.5 (10.5-45.8)	33.7±6.6 (19.6-47.0)	0.002
Platelets (x10 3)	317±145 (293; 71-767)	294±99 (78-641)	343±183 (71-767)	0.206
INR	1.1±0.2 (1.0; 0.9-1.8)	1.1±0.2 (0.9-1.8)	1.1±0.1 (1.0 -1.4)	0.219
Time between the decision of perioperative transfusion and the start (min)	58±20 (61; 15-95)	61±10 (47-75)	56±24 (15-95)	0.512
Total transfusion time (hours)	5.3±1.0 (5.6; 1.8-6.0)	5.1±1.1 (1.9-6.0)	5.4±0.9 (1.8-6.0)	0.214
When the transfusion is started				
BP (mmHg)				
systolic	108±15 (106; 70-138)	105±14 (70-129)	110±16 (75 -138)	0.211
diastolic	65±10 (66.5; 40-86)	65±10 (40-80)	65±10 (44-86)	0.877
heart rate (/ min)	87±14 (87; 60-131)	86±14 (62-130)	88±15 (60-114)	0.672
shock index	0.8±0.2 (0.8; 0.5-1.4)	0.8±0.2 (0.6-1.4)	0.8±0.2 (0.5 -1.2)	0.605
Hb (g/dl)	8.7±2.5 (9.2; 2.4-13.8)	7.7±2.8 (2.4 -13.8)	9.7±1.5 (6.2-11.9)	0.002
HTC (%)	27.7±7.0 (28.1; 10.5-39.6)	25.0±7.7 (10.5-39.6)	30.7±4.6 (19.7-38.9)	0.002
Platelets (x10 3)	262±115 (233; 78-767)	237±80 (78-474)	291±143 (108-767)	0.077
INR	1.1±0.2 (1.1; 0.9-1.8)	1.0±0.1 (0.9-1.3)	1.2±0.2 (1.0-1.5)	0.001
During hospital stay				
lowest Hb (g/dl)	7.1±20. (7.0; 2.4-10.9)	6.6±2.1 (2.4 -10.8)	7.7±1.7 (5.5 -10.9)	0.047
lowest HTC (%)	22.5±5.0 (22.9; 10.5-33.6)	21.7±5.8 (10.5-33.6)	23.3±3.8 (17.2-29.9)	0.256
lowest Platelet (x10^3)	192±115 (173; 23-764)	188±74 (39-464)	196±150 (23 -764)	0.794
highest INR	1.3±0.5 (1.1; 0.9-4.3)	1.1±0.2 (0.9-2.0)	1.4±0.6 (1.0-1.7)	0.045
On discharge				
Hb (g/dl)	10.1±1.1 (10.2; 7.9-13.3)	9.8±0.9 (7.9-11.7)	10.3±1.3 (8.0-13.3)	0.135
HTC (%)	31.8±3.4 (31.5; 24.8-42.6)	31.1±2.5 (25.0-36.9)	32.5±4.1 (24.8-42.6)	0.106
Platelets (x10 3)	327±177 (256; 114-877)	253±95 (134 -510)	415±211 (114-877)	0.001
INR	1.1±0.1 (1.0; 0.9-1.6)	1.0±0.1 (0.9-1.3)	1.1±0.1 (0.9-1.6)	0.031
Length of stay in intensive care (days)	2.4±2.2 (1; 1-7)	1.1±0. 4 (1-2)	2.9±2.4 (1-7)	0.006
Length of stay in hospital (days)	9.7±6.7 (8; 2-29)	6.4±4.4 (2-20)	13.5±7.0 (4-29)	<0.001

Table 2. Distrubition of diagnoses (n=56)

Hospitalization diagnoses	n
Gynecology cases (n=30)	
Severe anemia (Hemoglobine <7 g/dl) + gynecological pathology (abnormal uterine bleeding; myoma uteri)	14
Myoma uteri	8
Adnexal mass	4
Intraabdominal bleeding (ectopic pregnancy rupture, ovarian cyst rupture)	2
Postmenopausal bleeding	one
Uterine prolapse	one
Gynecological oncology cases (n=26)	
Ovarian cancer	14
Endometrial cancer	5
Recurrent gynecological malignancy	3
Uterine sarcoma	2
Suspected adnexal mass	2

The most common blood groups were O (+) (n=18, 32.1%) and A (+) (n=16, 28.6%) among cases. (**Table 3**). While the amounts of erythrocyte suspension given were similar between the two patient groups (5.1±1.4 vs. 6.3±3.5 U, p=0.082), FFP amounts were higher in the gynecologic oncology group (3.3±2.0 vs. 6.2±3.7 U, p=0.001). Pooled platelet transfusion was performed in only 2 of 56 cases (1 U in 1 case, 2 U in 1 case) and cryoprecipitate (40 U) in one patient. The amount of fibrinogen is also significantly higher in gynecological oncology cases (p=0.037) (**Table 4**).

Table 3. Distribution of cases in terms of blood group

ABO	Rh / rh Antigen	n	%
HE	- +	3 18	5.4 32.1
A	- +	3 16	5.4 28.6
B	- +	one 10	1.8 17.9
EU	- +	- 5	8.9

Table 4. Amounts of blood products transfused

	All cases (n=56)	Gynecology cases (n= 30)	Gynecological oncology cases (n=26)	p
	Mean±SD (Median; min-max)	Mean±SD (min-max)		
Erythrocyte suspension (U)	5.6±2.7 (5; 4-17)	5.1±1.4 (4-9)	6.3±3.5 (4-17)	0.082
Fresh frozen plasma (U)	4.7±3.2 (4; 1 -15)	3.3±2.0 (1-8)	6.2±3.7 (2-15)	0.001
Fibrinogen (gr)	2.4±1.0 (2; 1-6)	2.1±0.8 (1-4)	2.8±1.1 (1-6)	0.037

When the allergic reaction and transfusion-related complications in the cases who received massive blood transfusion are examined, febrile nonhemolytic transfusion reaction (high fever; >38°C) that was controlled with medication in 5 patients at the time of transfusion, acute hemolytic transfusion reaction in 2 cases (fever, chills chest and back/ low back pain) and an allergic reaction (dyspnea, urticaria) was detected in 1 case. In these cases, transfusion was temporarily suspended and continued after medication. In one case, the transfusion was terminated due to uncontrollable fever. Anaphylactic reaction (angioedema, hypotension and wheezing) was detected during transfusion in 1 case, the reaction was terminated and medical treatment was started. In 1 case, the diagnosis of Transfusion-related acute lung injury (TRALI) based on the examination performed on the development of respiratory distress, hypoxia, and hypotension during transfusion and the findings of abnormal chest X-ray, and in 1 case, dyspnea, respiratory distress, and development of hypoxia in the lungs after the end of the transfusion. A diagnosis and treatment of transfusion-associated circulatory overload (TACO) was made based on the findings on chest X-ray and abnormal chest X-ray. Two patients who developed TRALI and TACO were also gynecological oncology cases. The duration of stay in the intensive care unit and hospitalization of gynecological oncology cases was significantly longer. 1 of 56 patients who underwent massive blood transfusion died (gynecological oncology case).

DISCUSSION

In this study, the frequency of blood transfusion meeting the criteria for massive blood transfusion to patients receiving treatment in gynecological and gynecological oncology clinics in a tertiary center was 1.78%. When the need for blood transfusion is discussed in surgical clinics, it is thought that transfusion is needed because of bleeding secondary to the surgery performed first. However, cases may present with severe anemia (Hb <7 g/dl) due to abnormal bleeding originating from the uterus, which are especially specific to the gynecology clinic, and these cases may require transfusion up to massive transfusion regardless of surgery. In our study, out of a total of 56 patients who underwent massive blood transfusion, 28.6% (n=16) received massive blood transfusion regardless of surgery. Severe anemia was found in 14 of them due to severe abnormal uterine bleeding. Unless these patients have a known malignant disease, they are primarily treated in gynecology clinics due to severe anemia. These cases are also predominantly pre- and perimenopausal women. Thus, the mean age of the cases who underwent massive blood transfusion in the gynecology clinic was found to be significantly lower than the gynecological oncology group (44.6±10.4 vs. 54.3±9.4, p=0.001). In addition, hemoglobin levels at hospitalization were significantly lower in this group (8.1±3.4 vs. 10.7±2.2; p=0.002).

In our study, vital signs, shock indices, and total transfusion times of the cases were found to be similar between the groups during the perioperative decision to transfusion. This proves that there is a standard management among clinics in terms of approach to bleeding and patient blood management in our hospital.

In a study evaluating the knowledge levels of healthcare professionals about the transfusion of blood products, it was found that 60% of the questions about blood product transfusion of healthcare personnel working in our hospital were answered correctly. The highest correct response rate (73%, n: 66) was found in the field of basic transfusion information, while the least (47%, n:45) correct response rate was obtained in the storage of blood products. However, it was found that the level of knowledge about basic information and the storage of blood products did not differ between doctors and nurses or between internal and surgical clinics.[3] Knowledge and awareness about the subject is critical for the prevention of complications. To prevent errors that may arise in determining the suitability of donor components for the recipient; At the same time, it is the responsibility of the doctor and nurse who takes care of the patient to recognize the transfusion reactions and to apply the most appropriate treatment in a short time. It is defined as side effects observed during transfusion or within the

first 24 hours. Acute transfusion complications can be classified as immunological and non-immunological. Immunological transfusion reactions occur when transfused erythrocytes, leukocytes, platelets and plasma proteins stimulate antibody production in the recipient. Non-immunological reactions, on the other hand, occur due to the physical and chemical properties of the transfused blood product.[4] Rapidly transfusing large amounts of blood may cause hyperkalemia in the patient. This is more common in patients with renal failure, acidosis with shock, and hemolysis. Citrate, which is used as an anticoagulant in blood products, is metabolized in the liver. The amount of citrate increases in massive transfusion, hepatic failure and shock. Increased citrate level may also lead to mortal complications due to hypocalcemia.[4,5]

In the applications of massive blood transfusion, the general acceptance is to provide the replacement of blood content at a ratio of 1:1:1 (Erythrocyte suspension (ES): Fresh frozen plasma (FFP): Pooled platelets).[6,7] This concept is critical due to the fact that, coagulation factors and platelets are consumed simultaneously as well as the loss of erythrocyte mass during massive bleeding.[8-10] However, in our study, the ratio of ES / FFP was not 1:1 especially in gynecology cases. The reason is that severe anemia in a significant part of these cases develops as a result of a process due to severe abnormal uterine bleeding without being secondary to surgery, therefore coagulopathy does not develop and it will be sufficient to correct anemia and hypovolemia with ES replacement, even in massive amounts.[11,12] However, in this case, as a complication of massive ES transfusion without FFP administration, the development of dilutional coagulopathy by reducing the existing coagulation factors and platelets, development of hypocalcemia due to citrate toxicity and development of hyperkalemia should be vigilant.[10,13] In gynecological oncology cases, it is noteworthy that 1:1 ratio is achieved in ES/FTP. The reason for this is that replacements are made considering that coagulation factors are consumed along with erythrocyte loss during perioperative surgery.[14] Likewise, fibrinogen supplementation is used more in gynecological oncology cases. Thrombocyte replacement was performed in only 2 cases because the thrombocyte count decreased below 50 thousand during transfusion.[15,16]

Perioperative blood transfusion is associated with increased morbidity and prolonged length of stay in hospital.[17,18] In a study evaluating the incidence of perioperative blood transfusion and association with 30 day postoperative outcomes in gynecologic cancer surgery (n=62 531), the overall incidence of transfusion was found to be 9.4%. On multivariable analysis, blood transfusion was predictive of composite morbidity (adjusted odds ratio (OR) 1.65, 95% confidence interval (CI) 1.48 to 1.85) and length of stay in hospital ≥5 days (adjusted OR 9.02, 95% CI 8.21 to 9.92). Perioperative blood transfusion was the most predictive factor for composite morbidity (adjusted OR 1.67, 95% CI 1.35 to 2.07) and length of stay in hospital ≥7 days (adjusted OR 9.75, 95% CI 7.79 to 12.21).[19] Authors revealed that, preoperative patient optimization and local institutional practices should be reviewed to improve the use of blood bank resources and adherence to restrictive blood transfusion protocols.[19]

In a study comparing differences in blood transfusion and surgical complication rates before and after the implementation of a restrictive blood transfusion protocol in patients undergoing major abdominal surgery by the gynecology and gynecologic oncology services before, and after initiation of the transfusion protocol, a similar number of patients received blood transfusions in both groups (9.3% versus 10.6% p=0.57). However, significantly fewer units of blood were given post-protocol initiation. For every patient who received a transfusion pre-protocol, 2.66 units were administered compared to 1.2 units after the protocol was initiated (p=0.003). They claimed that a restrictive transfusion protocol is effective in decreasing the number of units of blood transfused without affecting postoperative complication rates in gynecologic surgery patients.[5]

CONCLUSION

In our study, especially in in massive hemorrhage secondary to perioperative surgery, the decision of transfusion was made at the stage when the patient's vital signs and coagulation factors could be compensated. In massive hemorrhages, while compensation mechanisms are still in effect, it is life-saving to make a timely decision for transfusion before hypovolemia symptoms and the severity of coagulopathy worsen.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Etlik City Hospital No: 1 Clinical Researches Ethics Committee (Date: 16.08.2023, AEŞH-EK1-2023-482).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

REFERENCES

1. Waters JH, Bonnet MP. When and how should I transfuse during obstetric hemorrhage?. *Int J Obstet Anesth.* 2021;46:102973. doi:10.1016/j.ijoa.2021.102973
2. Critical Bleeding/Massive Transfusion"; T.R. Ministry of Health, General Directorate of Health Services, Department of Blood and Blood Products, Patient Blood Management Guide: Module 1: Ankara, Ünlü A, Çetin AT, Yenicesu İ, Ertuğrul Örüç N, Balas Ş. January 2023; page: 26 [Internet: Patient Blood Management Guide: Module 1 (saglik.gov.tr)
3. Gökçebay D, Tekgündüz S, Yaşar S, Bolaç S, Işın U. Evaluation of hospital staff's awareness on blood product transfusion. *Academic Res Med.* 2016;3(1):100-105
4. Turkish Society of Hematology. Supportive therapies and infections in hematology course guide 2007:164-176.
5. Mojdehbakhsh RP, Al-Rubaye R, Huang DS, Connor J, Al-Niaimi A. Efficacy and safety of a restrictive blood transfusion protocol in gynecologic surgical patients. *Gynecol Oncol Rep.* 2022;43:101059. doi:10.1016/j.gore.2022.101059
6. Spahn DR, Goodnough LT. Alternatives to blood transfusion. *Lancet.* 2013;381(9880):1855-1865. doi:10.1016/S0140-6736(13)60808-9
7. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion.* 2017;57(6):1347-1358. doi:10.1111/trf.14006
8. Spahn DR. Patient Blood Management: the new standard. *Transfusion*. 2017;57(6):1325-1327. doi:10.1111/trf.14095
9. Pham HP, Shaz BH. Update on massive transfusion. *Br J Anaesth.* 2013;111 Suppl 1:i71-i82. doi:10.1093/bja/aet376
10. Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015;313(5):471-482. doi:10.1001/jama.2015.12
11. Mesar T, Larentzakis A, Dzik W, Chang Y, Velmahos G, Yeh DD. Association between ratio of fresh frozen plasma to red blood cells during massive transfusion and survival among patients without traumatic injury. *JAMA Surg.* 2017;152(6):574-580. doi:10.1001/jamasurg.2017.0098
12. Pham HP, Shaz BH. Update on massive transfusion. *Br J Anaesth.* 2013;111 Suppl 1:i71-i82. doi:10.1093/bja/aet376
13. Mesar T, Larentzakis A, Dzik W, Chang Y, Velmahos G, Yeh DD. Association between ratio of fresh frozen plasma to red blood cells during massive transfusion and survival among patients without traumatic injury. *JAMA Surg.* 2017;152(6):574-580. doi:10.1001/jamasurg.2017.0098
14. Zaidi A, Kohli R, Daru J, et al. Early use of fibrinogen replacement therapy in postpartum hemorrhage-a systematic review. *Transfus Med Rev.* 2020;34(2):101-107. doi:10.1016/j.tmrv.2019.12.002
15. Kovalic AJ, Khan MA, Malaver D, et al. Thromboelastography versus standard coagulation testing in the assessment and reversal of coagulopathy among cirrhotics: a systematic review and meta-analysis. *Eur J Gastroenterol Hepatol.* 2020;32(3):291-302. doi:10.1097/MEG.0000000000001588
16. Van Haren RM, Valle EJ, Thorson CM, et al. Hypercoagulability and other risk factors in trauma intensive care unit patients with venous thromboembolism. *J Trauma Acute Care Surg.* 2014;76(2):443-449. doi:10.1097/TA.0b013e3182a9d11d
17. Wise R, Bishop D, Gibbs M, et al. South African Society of Anaesthesiologists perioperative patient blood management guidelines. SAJAA. 2020;26:1-59. doi: 10.36303/SAJAA.2020.26.6.S1
18. Lopez-Picado A, Albinarrate A, Barrachina B. Determination of perioperative blood loss: accuracy or approximation?. *Anesth Analg.* 2017;125(1):280-286. doi:10.1213/ANE.0000000000001992
19. Swift BE, Maeda A, Bouchard-Fortier G. Adverse postoperative outcomes associated with perioperative blood transfusion in gynecologic oncology surgery. *Int J Gynecol Cancer.* 2023;33(4):585-591. doi:10.1136/ijgc-2022-004228